nature reviews endocrinology

https://doi.org/10.1038/s41574-025-01157-1

Review article

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Advances in the management of hyperglycaemia and diabetes mellitus during hospitalization

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Abstract

Diabetes mellitus, which affects over 537 million people worldwide, considerably increases the risk of emergency room visits and admissions to hospital. Inpatient hyperglycaemia in patients with or without diabetes mellitus is associated with higher rates of complications, extended hospital stays and increased mortality when compared with patients with normoglycaemia. The American Diabetes Association recommends a target range of 5.6–10.0 mmol/l (100–180 mg/dl) for levels of glucose in the blood of patients in intensive care units (ICUs), as well as in general medicine and surgery. Insulin therapy remains the cornerstone of managing inpatient hyperglycaemia, with intravenous insulin preferred in ICU and basal–bolus regimens favoured in non-ICU settings. While bedside capillary blood glucose monitoring is standard for adjusting insulin doses, continuous glucose monitoring provides a more comprehensive glycaemic assessment and enhances the prevention of hypoglycaemia in high-risk hospitalized patients. This Review outlines the latest evidence in managing diabetes mellitus and hyperglycaemia within hospitals.

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Key points

- Dysglycaemia is common in intensive care unit (ICU) and non-ICU settings; both hyperglycaemia and hypoglycaemia are associated with poor outcomes.
- Glycaemic targets vary according to hospital settings, but maintaining tight control (5.6–10.0 mmol/l (100–180 mg/dl)) of blood levels of glucose in general wards and less strict control (<10 mmol/l (180 mg/dl)) in ICU settings is recommended.
- In the ICU setting, a variable rate intravenous insulin infusion is the preferred approach to achieve and maintain glycaemic targets.
- Glucose management in general wards can be achieved using basal–bolus or basal-plus insulin regimens, or by oral anti-diabetes medications.
- It is important that the transition from intravenous insulin infusion to a scheduled subcutaneous insulin regimen is effectively managed to prevent rebound hyperglycaemia.
- Continuous glucose monitoring in hospitals provides accurate readings and has the potential to enhance glycaemic metrics.

Introduction

Inpatient hyperglycaemia is defined by the American Diabetes Association (ADA), the Endocrine Society, and the Joint British Diabetes Societies for Inpatient Care (JBDS-IP) group as any glucose concentration of >7.8 mmol/l (140 mg/dl) in hospitalized patients[1–3]. Inpatient hyperglycaemia is found in the settings of known diabetes mellitus or previously undiagnosed diabetes mellitus, and in patients with or without diabetes mellitus who can develop stress-associated hyperglycaemia in response to physiological stress (such as surgery and other procedures, metabolic stress, medication and anaesthesia)[4]. It is estimated that 20–30% of adults with stress hyperglycaemia have diabetes mellitus that was previously undiagnosed, and up to 60% will have impaired glucose tolerance during follow-up[5]. Clinical guidelines recommend that any inpatient who presents with blood levels of glucose of >7.8 mmol/l (140 mg/dl) be assessed with a glycated haemoglobin (HbA_{1c}) test if one has not been performed in the preceding 2–3 months[1,2]. For those with known diabetes mellitus, the measurement of HbA_{1c} during hospitalization helps to identify individuals who might need intensified glycaemic management; in people with newly recognized hyperglycaemia, HbA_{1c} values can differentiate those with previously undiagnosed diabetes mellitus from those with stress-induced hyperglycaemia, as the test measures the amount of glucose attached to haemoglobin over the past 2–3 months[1].

Several observational studies and meta-analyses have consistently shown that hyperglycaemia and diabetes mellitus in intensive care units (ICU) and non-ICU settings are associated with poor clinical outcomes. These poor outcomes include a longer hospital stay, higher readmission rates, and increased rates of morbidity and mortality compared with inpatients with normoglycaemia[6–10]. A large retrospective study of over 250,000 critically ill patients in the USA found that a glucose concentration of >6.1 mmol/l (110 mg/dl) independently increased the risk of mortality in individuals with and without diabetes mellitus admitted to hospital with cardiac conditions, sepsis or respiratory failure[6]. Similarly, in a prospective cohort multicentre study of 2,471 individuals with community-acquired pneumonia, those with a glucose level of >11.1 mmol/l (200 mg/dl) on admission to hospital had a greater risk of mortality and complications, with an estimated increased risk of 3% for each 1.0 mmol/l (18 mg/dl) increase in glucose level on admission, than those with a glucose level of <11.1 mmol/l (200 mg/dl)[11]. In general surgery, patients with diabetes mellitus with a glucose level of >11.1 mmol/l (200 mg/dl) had a twofold higher risk of postoperative mortality compared with those with a glucose level of <5.6 mmol/l (100 mg/dl)[7]. Moreover, the risk of postoperative infections in general surgery has been reported to increase by 30% for every 2.2 mmol/l (40 mg/dl) rise in glucose level above normoglycaemia[12].

Early identification of elevated glucose levels and subsequent intervention can decrease hyperglycaemia and hospital complications[13]. In 2024, a randomized controlled trial of 1,371 admissions showed that early intervention with an electronic specialist-led diabetes mellitus 'proactive' model of care reduced glucose levels and the number of health-care-associated infections compared with those who received standard diabetes mellitus care[14]. This strategy also resulted in lower median patient-day mean glucose levels of 8.2 mmol/l (147.6 mg/dl) compared with 8.6 mmol/l (154.8 mg/dl) in the control group ($P < 0.0001$)[14]. Patients experiencing new-onset or stress hyperglycaemia of >7.8 mmol/l (140 mg/dl) during periods of illness also exhibit higher rates of hospital complications and mortality than those with a history of diabetes mellitus[15]. However, it remains unclear whether hyperglycaemia directly causes these adverse outcomes or functions as a marker of stress and disease severity, and whether correcting stress-related hyperglycaemia can effectively improve clinical outcomes and reduce hospital complications[16].

Robust observational data indicate that inpatient hypoglycaemia, defined as glucose <3.9 mmol/l (70 mg/dl), is also associated with an increased risk of morbidity and mortality[17,18]. Patients with insulin-induced hypoglycaemia and those with spontaneous hypoglycaemia show higher rates of mortality and complications than patients without hypoglycaemia. Interestingly, current evidence indicates a higher mortality rate in patients admitted with spontaneous hypoglycaemia compared with the rate in those with insulin-induced hypoglycaemia, implying that hypoglycaemia itself might not directly cause poor outcomes but, rather, functions as an indicator of underlying disease severity[19].

Given the increased risk of morbidity and mortality associated with hyperglycaemia, hypoglycaemia and glycaemic variability, a comprehensive and multistep regimen is recommended for managing glycaemic control in hospitalized patients[20]. This regimen includes implementing dietary recommendations, structured glucose monitoring plans, personalized glycaemic targets and treatment approaches to control hyperglycaemia while minimizing hypoglycaemia. In this Review, we aim to provide an overview of relevant evidence on the management of diabetes mellitus and hyperglycaemia in the hospital setting.

Glycaemic targets in hospitalized patients with diabetes mellitus

Glycaemic control in hospitalized patients is essential for improving outcomes and reducing complications. The following sections outline glycaemic targets for critically ill patients in the ICU and those receiving care in general wards.

Table 1 | Guidelines from the major societies for treatment of hyperglycaemia in ICU and non-ICU settings

Society	ICU setting	Non-ICU setting
AACE–ADA[26]	Initiate insulin therapy for persistent hyperglycaemia (glucose >10 mmol/l (180 mg/dl)); target glucose level of 7.8–10.0 mmol/l (100–180 mg/dl) in most people; 6.1–7.8 mmol/l (110–140 mg/dl) might be appropriate in selected individuals (critically ill postsurgical, cardiac surgery), if achievable without notable hypoglycaemia	Initiate insulin therapy for persistent hyperglycaemia (glucose >10 mmol/l (180 mg/dl)); target glucose level of 7.8–10.0 mmol/l (100–180 mg/dl) in most people
American College of Physicians[114]	Recommends against intensive insulin therapy to normalize blood levels of glucose in patients in the ICU setting with or without diabetes mellitus; target glucose level of 7.8–11.1 mmol/l (140–200 mg/dl) in insulin-treated patients in the ICU setting	Recommends against intensive insulin therapy to strictly control blood levels of glucose in patients in non-ICU settings with or without diabetes mellitus; no specific glucose targets in non-ICU settings; target levels <7.8–11.1 mmol/l (140–200 mg/dl) should be avoided
Critical Care Society[115]	Blood glucose levels >8.3 mmol/l (150 mg/dl) should trigger insulin therapy; maintain glucose <8.3 mmol/l (150 mg/dl) in most adults in the ICU setting; maintain glucose levels <10.0 mmol/l (180 mg/dl) while avoiding hypoglycaemia	NA
Endocrine Society[1]	NA	Pre-meal blood glucose target of <7.8 mmol/l (140 mg/dl) and random blood glucose <10.0 mmol/l (180 mg/dl); a lower target range might be appropriate in people able to achieve and maintain glycaemic control without hypoglycaemia; a target of <11.1 mmol/l (200 mg/dl) is appropriate in those with terminal illness and/or with limited life expectancy or at high risk of hypoglycaemia; adjust anti-diabetes therapy when glucose levels fall to <5.6 mmol/l (100 mg/dl) to avoid hypoglycaemia
Society of Thoracic Surgeons (guidelines specific to adult cardiac surgery)[116]	Continuous intravenous insulin infusion preferred over subcutaneous or intermittent intravenous boluses; recommend glucose levels <10.0 mmol/l (180 mg/dl) during surgery	NA
JBDS-IC[29]	NA	Target blood levels of glucose in most people of 6.0–10 mmol/l (110–180 mg/dl) with an acceptable range of 4.0–11.9 mmol/l (70–215 mg/dl); perioperative target blood glucose level of 6.0–10 mmol/l (110–180 mg/dl) with acceptable range up to 11.9 mmol/l (215 mg/dl)
American Society of Parenteral and Enteral Nutrition[117]	Target blood glucose range 7.8–10 mmol/l (140–180 mg/dl) in people receiving nutrition support	Target blood glucose range 7.8–10 mmol/l (140–180 mg/dl) in people receiving nutrition support
Society for Ambulatory Anesthesia[118]	Initiate insulin therapy for blood levels of glucose >10 mmol/l (180 mg/dl); in most people, target glucose level of 7.8–10 mmol/l (140–180 mg/dl)	If treated with insulin, pre-meal glucose targets should generally be <7.8 mmol/l (140 mg/dl), with random glucose levels <10 mmol/l (180 mg/dl)
Surviving Sepsis Campaign 2021 (ref. 119)	Initiate insulin therapy for blood levels of glucose >180 mg/dl (10 mmol/l); in most people, target glucose level of 140–180 mg/dl (7.8–10 mmol/l)	NA

AACE–ADA, American Association of Clinical Endocrinologists and American Diabetes Association joint guidelines; ICU, intensive care unit; JBDS-IC, Joint British Diabetes Societies for Inpatient Care; NA, not available. Adapted with permission from ref. 42, Wolters Kluwer.

ICU settings

The recommended target levels of glucose in the blood for individuals in the ICU setting, according to various society guidelines, are shown in Table 1. Over the past two decades, randomized controlled trials have shown conflicting results regarding the benefits of achieving near-normoglycaemia in the ICU setting compared with a more liberal control of blood levels of glucose (Table 1). In 2001, a single-centre surgical ICU study found a 42% relative reduction in mortality when the levels of glucose in the blood were normalized to 4.4–6.1 mmol/l (80–110 mg/dl) following intensive insulin therapy compared with conventional treatment, drawing global attention and prompting professional organizations to recommend intensive control of levels of glucose in the ICU setting[21]. However, subsequent multicentre randomized controlled trials and meta-analyses of patients with and without diabetes mellitus consistently showed a lack of benefit of intensive glycaemic control along with unacceptably high rates of hypoglycaemia following intensive insulin therapy. A 2024 meta-analysis that included 14,171 participants from 20 trials concluded that intensive control of glucose in the blood in critically ill adults did not lower the risk of mortality but instead led to a higher incidence of hypoglycaemia compared with conventional glucose control[22]. Subgroup analysis, considering factors such as sex, ICU admission type, presence of diabetes mellitus, use of corticosteroids and other variables, also showed no difference in mortality rates between intensive and conventional glucose control[22]. Moreover, in the NICE-SUGAR (Normoglycaemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation) study, a tight target level of glucose in the blood was associated with higher mortality rates than a moderate target[23]. NICE-SUGAR was a multicentre clinical trial that included 6,104 adult patients admitted to medical and surgical ICUs randomized to receive intensive control (4.5–6 mmol/l (81–108 mg/dl)) or conventional control (10 mmol/l (180 mg/dl)) of blood levels of glucose to determine the optimal glucose target

range in the hospital[23]. On the other hand, in another study, in which 9,230 patients were randomized to liberal glucose control and 4,608 to tight glucose control in the ICU setting (not receiving total parenteral nutrition, which can increase the severity of hyperglycaemia), tight control did not affect the mortality or the length of time for which ICU care was required[24]. Accordingly, recommendations from clinical societies advise that, although glucose management is essential, a less strict approach is acceptable, suggesting a glucose target of ≤10 mmol/l (180 mg/dl)[25]. ADA guidelines were updated in 2025, and recommend a glycaemic goal of 7.8–10.0 mmol/l (140–180 mg/dl) for most critically ill patients, while allowing for an individualized target of <7.8 mmol/l (140 mg/dl) if it can be accomplished without hypoglycaemia[3].

Non-ICU settings

For non-critically ill individuals, the American Association of Clinical Endocrinology guidelines for the management of hyperglycaemia in the non-critical care setting recommend a target level of glucose in the blood of <7.8 mmol/l (140 mg/dl) for fasting and <10.0 mmol/l (180 mg/dl) for random blood glucose values[26]. The ADA 'Standards of Care in Diabetes' and the Endocrine Society recommend targets of 5.6–10.0 mmol/l (100–180 mg/dl) in most people in general medicine or general surgery settings[27,28]. Similarly, guidelines from the JBDS-IP group in the UK recommend a target range of glucose levels in the blood of 5.6–10.0 mmol/l (100–180 mg/dl), with an acceptable range of 4.9–11.1 mmol/l (70–200 mg/dl)[29]. It should be noted that the lower target might increase the risk of hypoglycaemia[30], and no prospective trials have identified an ideal target for the management of hyperglycaemia in non-critically ill individuals with diabetes mellitus. In patients with organ failure, such as advanced kidney disease (and/or those on dialysis), those who are terminally ill or those at risk for hypoglycaemia, glucose levels up to 250 mg/dl (13.9 mmol/l) might be allowed[3].

Treating hyperglycaemia and diabetes mellitus in the hospital setting

Professional societies recommend insulin therapy as the cornerstone of pharmacological management in hospitalized patients with diabetes mellitus. Continuous administration of insulin via intravenous infusion is the preferred method to achieve glycaemic targets in patients who are critically ill or with hyperglycaemic crises[31]. In general medicine and surgery settings, clinical guidelines recommend the use of insulin, administered subcutaneously, over non-insulin regimens[1,2]; however, increasing evidence indicates that an individualized approach based on diabetes mellitus treatment prior to admission and the severity of hyperglycaemia is the best way to achieve glycaemic control while avoiding the risk of iatrogenic hypoglycaemia[32,33]. Examples of individualization include avoiding tight control in a person with multiple comorbidities or allowing patients well-controlled with excellent time in range on continuous subcutaneous insulin infusions (pumps) to continue with tight glycaemic control if they wish and can do so[32,33].

ICU settings

In critically ill individuals, a variable-rate intravenous insulin infusion is the preferred approach for achieving and maintaining glycaemic targets. The short half-life of insulin makes the intravenous route ideal because of the flexibility, in terms of dosage, that can be offered in the event of unpredictable changes in an individual's health, medications and nutrition.

Three essential elements increase the success of continuous intravenous insulin infusion in the ICU: rate adjustment is based on the current and previous glucose values and the current rate of insulin infusion; rate adjustment considers the rate of change (or lack of change) from the previous reading; and glucose monitoring is carried out every 1–2 h (ref. 32). Several nurse-driven intravenous insulin infusion protocols are effective for achieving glycaemic control and improving hospital outcomes, with a low rate of hypoglycaemic events[34,35]. Several computer-based algorithms designed to guide the nursing staff in adjusting insulin infusion rates are commercially available[36,37]. Observational and prospective controlled trials have shown faster, tighter glycaemic control and lower glycaemic variability using computer-guided algorithms compared with standard paper-form protocols in the ICU[36,37]. Most computer-guided insulin algorithms are appropriate for managing hyperglycaemia in the ICU setting, and the choice depends upon the physician's preference or level of comfort, institutional availability and cost considerations[38–40]. An example of a variable-rate continuous insulin infusion algorithm (used at Emory University School of Medicine) is shown in Fig. 1 (refs. 41,42).

The use of subcutaneous insulin injection has not been formally studied in the ICU setting. However, it should be avoided in critical illness during states of arterial hypotension or shock, or when using inotropes that cause peripheral vasoconstriction, as these conditions limit insulin uptake owing to impaired tissue perfusion and unpredictable absorption. Many factors can affect insulin absorption and action during critical illness and/or perioperatively, and these factors might worsen glycaemic control. An observational study in the ICU setting showed lower mean daily blood levels of glucose, a lower proportion of hypoglycaemic and hyperglycaemic events, and a greater percentage of blood glucose readings within a target range of 3.9–10 mmol/l (70–180 mg/dl) following intravenous insulin infusion compared with subcutaneous insulin injection regimens[43].However, a retrospective evaluation of a subcutaneous insulin protocol in patients with diabetic ketoacidosis at 21 centres in northern California, USA, with a total of 7,989 hospitalizations over 9 years, showed a 57% reduction in the need for ICU admission and a 50% reduction in 30-day hospital readmission compared with standard care using intravenous insulin in the ICU in the control group. No notable differences in hospital length of stay or mortality rates were observed between the treatment groups[44].

Transitioning from intravenous to subcutaneous insulin regimen (from ICU to general medicine or surgery)

During the post-acute phase, transition orders from an intravenous insulin infusion to a scheduled subcutaneous insulin regimen are needed to prevent rebound hyperglycaemia, which can occur if the transition occurs with a short overlap period with intravenous insulin or if the dose calculation is inaccurate. This approach is imperative in patients with type 1 diabetes mellitus, as stopping or delaying insulin for only a few hours can result in severe hyperglycaemia and diabetic ketoacidosis. Several studies have recommended switching from intravenous to subcutaneous insulin when patients begin eating regular meals or move to a lower-intensity care setting.

Most patients who have not previously been treated with insulin or who have no history of diabetes mellitus but required insulin infusion at low doses (≤2 units/h) in the ICU can be treated with correction doses of subcutaneous rapid-acting insulin (sliding scale) without basal insulin after being transitioned to non-ICU wards[42,45]. For patients who received high doses of intravenous insulin (>2 units/h) in the ICU setting or who were treated with insulin therapy before admission, the daily insulin dose could be based on their home regimen or the intravenous insulin requirements in the ICU[42,45,46]. Our institution recommends

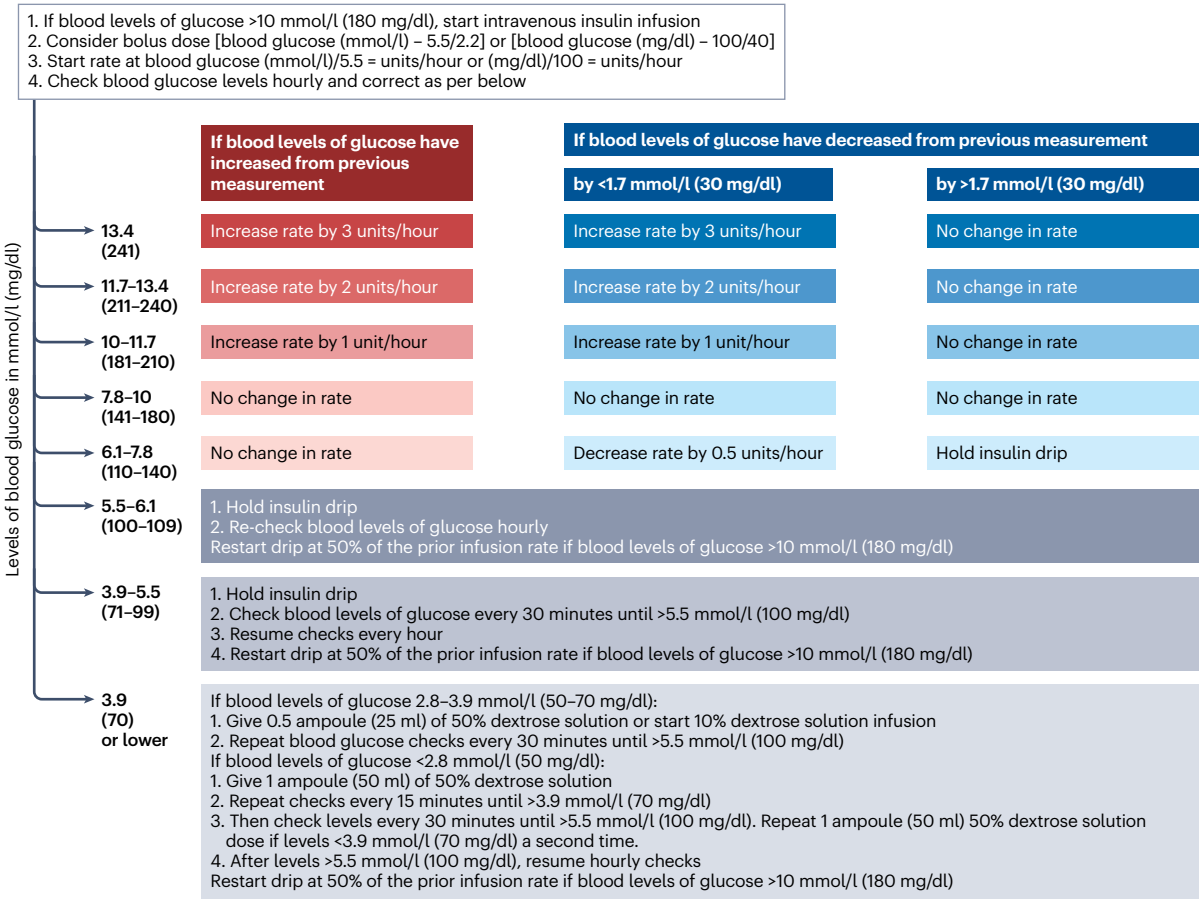
1. If blood levels of glucose >10 mmol/l (180 mg/dl), start intravenous insulin infusion
2. Consider bolus dose [blood glucose (mmol/l) – 5.5/2.2] or [blood glucose (mg/dl) – 100/40]
3. Start rate at blood glucose (mmol/l)/5.5 = units/hour or (mg/dl)/100 = units/hour
4. Check blood glucose levels hourly and correct as per below
Levels of blood glucose in mmol/l (mg/dl)
If blood levels of glucose have increased from previous measurement
If blood levels of glucose have decreased from previous measurement
by <1.7 mmol/l (30 mg/dl)
by >1.7 mmol/l (30 mg/dl)
13.4 (241)
Increase rate by 3 units/hour
Increase rate by 3 units/hour
No change in rate
11.7–13.4 (211–240)
Increase rate by 2 units/hour
Increase rate by 2 units/hour
No change in rate
10–11.7 (181–210)
Increase rate by 1 unit/hour
Increase rate by 1 unit/hour
No change in rate
7.8–10 (141–180)
No change in rate
No change in rate
No change in rate
6.1–7.8 (110–140)
No change in rate
Decrease rate by 0.5 units/hour
Hold insulin drip
5.5–6.1 (100–109)
1. Hold insulin drip
2. Re-check blood levels of glucose hourly
Restart drip at 50% of the prior infusion rate if blood levels of glucose >10 mmol/l (180 mg/dl)
3.9–5.5 (71–99)
1. Hold insulin drip
2. Check blood levels of glucose every 30 minutes until >5.5 mmol/l (100 mg/dl)
3. Resume checks every hour
4. Restart drip at 50% of the prior infusion rate if blood levels of glucose >10 mmol/l (180 mg/dl)
3.9 (70) or lower
If blood levels of glucose 2.8–3.9 mmol/l (50–70 mg/dl):
1. Give 0.5 ampoule (25 ml) of 50% dextrose solution or start 10% dextrose solution infusion
2. Repeat blood glucose checks every 30 minutes until >5.5 mmol/l (100 mg/dl)
If blood levels of glucose <2.8 mmol/l (50 mg/dl):
1. Give 1 ampoule (50 ml) of 50% dextrose solution
2. Repeat checks every 15 minutes until >3.9 mmol/l (70 mg/dl)
3. Then check levels every 30 minutes until >5.5 mmol/l (100 mg/dl). Repeat 1 ampoule (50 ml) 50% dextrose solution dose if levels <3.9 mmol/l (70 mg/dl) a second time.
4. After levels >5.5 mmol/l (100 mg/dl), resume hourly checks
Restart drip at 50% of the prior infusion rate if blood levels of glucose >10 mmol/l (180 mg/dl)

Fig. 1 | Perioperative algorithm. This algorithm outlines the use of variable rate intravenous insulin infusion for the management of patients with hyperglycaemia at Emory University, Atlanta, GA[41,42]. Adapted with permission from ref. 42, Wolters Kluwer.

calculating the total daily dose of insulin based on the insulin infusion requirement to maintain euglycaemia over the previous 8–12 h, starting with 60–80% as a subcutaneous basal dose, and starting prandial insulin when the individual can tolerate a regular diet. Basal insulin should be given 1–2 h before discontinuing the intravenous insulin infusion to decrease the risk of rebound hyperglycaemia and help reduce intravenous insulin requirements[46]. Patients who received non-insulin anti-diabetes medications at home but required intravenous insulin treatment in the hospital can be transitioned to subcutaneous insulin according to their insulin requirements and HbA_{1c} levels on admission. If not contraindicated, treatment with oral agents, such as dipeptidyl peptidase 4 (DPP4) inhibitors[47–51], can also be (re)started during the transition in addition to subcutaneous basal insulin. The use of DPP4 inhibitors, either alone or in combination with basal insulin, is safe and efficacious[48,49]. In patients with hyperglycaemia and heart failure, the ADA guidelines recommend that treatment with a sodium–glucose cotransporter 2 inhibitor (SGLT2i) should be initiated or continued, unless contraindicated, alongside basal subcutaneous insulin[52,53].

Treatment of hyperglycaemia in non-ICU settings

Clinical guidelines recommend administering subcutaneous insulin as the preferred therapeutic agent for glucose control in general medicine and surgical settings[1,54]. However, no single insulin regimen meets the needs of all individuals with hyperglycaemia in these settings[1,28]. Therefore, an individualized approach that incorporates patient characteristics (duration of diabetes mellitus and presence of comorbidities), severity of inpatient hyperglycaemia, and diabetes mellitus treatment before admission is recommended[32,33]. For insulin-naive individuals or those using low doses of insulin admitted with mild hyperglycaemia of <10.0 mmol/l (180 mg/dl), a low-intensity regimen of oral anti-diabetes agents or correction doses of rapid-acting insulin (sliding scale) might be appropriate[55]. A more intensive regimen is indicated in patients with severe hyperglycaemia and/or those treated with high-complexity regimens (multidose insulin plus either oral agents or non-insulin injectables) prior to admission[32]. Treatment options for the management of non-ICU patients with type 2 diabetes mellitus (T2DM) are summarized in Table 2.

Insulin therapy in non-ICU settings. Multiple regimens with human insulin and insulin analogues administered subcutaneously have been tested in non-critically ill patients with hyperglycaemia. Randomized controlled trials have consistently demonstrated better glycaemic control with a basal–bolus approach compared with the commonly used sliding scale insulin regimen in non-ICU patients with

Table 2 | Treatment options for the management of non-ICU patients with T2DM

Regimen	Indications	Contraindications
Correction with rapid-acting insulin alone	Stress hyperglycaemia (no history of diabetes mellitus), insulin-naive individuals with diabetes mellitus with mild hyperglycaemia of <10 mmol/l (180 mg/dl)	Patients with T1DM or those with T2DM with blood levels of glucose >11.1 mmol/l (200 mg/dl) or insulin treated prior to admission
Basal-plus (basal insulin plus correction with rapid-acting insulin)	General medicine or surgery patients previously treated at home with oral agents or low-dose insulin <0.6 units/kg/day	Patients with T1DM or those with T2DM on high-dose insulin regimen prior to admission
Basal–bolus insulin	Patients with T1DM and those with T2DM previously receiving complex regimen at home; severe hyperglycaemia; steroid-induced hyperglycaemia	Insulin-naive patients with mild hyperglycaemia of <11.1 mmol/l (200 mg/dl); nil-by-mouth or poor oral intake
Metformin	Continue therapy in stable patients on metformin prior to admission without contraindications and/or close to hospital discharge	Patients with T1DM or those with T2DM with kidney failure (eGFR <30 ml/min), worsening kidney function, heart failure, hypoxia or liver failure
Sulfonylureas	Not routinely recommended	Patients with T1DM or those with T2DM with kidney failure, frailty or poor oral intake
Thiazolidinediones	Not routinely recommended	Patients with T1DM or those with T2DM and heart failure
DPP4 inhibitors	General medicine or surgery patients with T2DM with mild hyperglycaemia of <11.1 mmol/l (200 mg/dl); combine with basal insulin if blood levels of glucose >11.1 mmol/l (200 mg/dl)	Patients with T1DM, history of pancreatitis, patients on high-dose insulin regimens
GLP1 receptor agonists	Not routinely recommended; limited evidence	Patients with T1DM or those with T2DM with a history of pancreatitis, multiple endocrine neoplasia, medullary thyroid carcinoma or gastrointestinal surgery
SGLT2 inhibitors	Potential benefit in patients with heart failure	Patients with T1DM or those with T2DM with eGFR <30 ml/min

DPP4, dipeptidyl peptidase 4; eGFR, estimated glomerular filtration rate; GLP1, glucagon-like peptide 1; SGLT, sodium–glucose cotransporter; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

hyperglycaemia[56,57]. A basal–bolus approach involves scheduled subcutaneous insulin therapy with basal insulin (glargine or degludec) once daily or neutral protamine Hagedorn (NPH) insulin twice daily, in combination with short (regular) or rapid-acting insulin (lispro, aspart, glulisine) before meals. In a surgical population, patients randomized to a basal–bolus approach compared with a sliding scale regimen showed a reduction in complications estimated with a composite that included postoperative wound infection, pneumonia, bacteraemia and acute renal and respiratory failure[58]. A regimen of sliding scale with regular insulin is effective for improving glycaemic control in patients with mild hyperglycaemia (<10.0 mmol/l (180 mg/dl)) who were treated with oral agents or low-dose insulin before admission; however, this approach is not effective as a single therapy in most patients with glucose levels of >10.0–11.1 mmol/l (180–200 mg/dl) on admission and should therefore be avoided[55].

Several studies have demonstrated that the basal–bolus approach is effective and safe for managing most people with T2DM in general surgery or medical settings[58–60]. Two randomized controlled trials in patients with T2DM in non-ICU settings compared the efficacy and safety of a basal–bolus regimen using insulin analogues (detemir, aspart, glargine and glulisine) or human insulin (NPH and regular insulin). These studies found similar glycaemic control but lower rates of hypoglycaemia using insulin analogues during hospitalization[39,61]. In another randomized controlled trial, premixed insulin therapy (70:30 formulation of NPH to regular insulin, administered twice daily) was compared with a basal–bolus regimen consisting of glargine once daily and glulisine before meals. This study found similar glucose control between the approaches; however, use of the premixed insulin formulation was associated with an unacceptably high rate of iatrogenic hypoglycaemia, and is not recommended for hospital use[62].

Most people in hospital experience reduced calorie intake owing to a lack of appetite, medical procedures or surgical intervention, putting them at risk of hypoglycaemia if they receive scheduled prandial subcutaneous insulin according to the basal–bolus regimen. In the 'basal-plus' trial, patients treated with low-dose insulin (≤0.4 units/kg/day), oral anti-diabetes agents or diet were randomized to receive one of three regimens: a standard basal–bolus regimen (starting at 0.4–0.5 units/kg/day) divided into 50% basal (glargine) and 50% bolus (glulisine); or a single daily dose of glargine (0.2–0.25 units/kg/day) with correction doses of rapid-acting insulin (glulisine) per sliding scale before meals for blood levels of glucose of >140 mg/dl (>7.8 mmol/l) (basal-plus); or sliding scale insulin alone[59]. In this study, the basal plus correction approach resulted in a similar improvement in glycaemic control compared with a standard basal–bolus regimen; both the basal–bolus and basal-plus regimens resulted in more favourable glycaemic control than did treatment with the sliding scale insulin approach. Thus, in insulin-naive patients or those receiving low-dose insulin on admission, those on oral agents or non-insulin injectables, or those with reduced calorie intake, using a basal plus correction regimen is an effective alternative to the basal–bolus regimen[59] (Fig. 2).

Finally, several randomized controlled trials have compared the efficacy and safety of different basal insulin analogues in non-ICU settings. These studies showed similar efficacy and safety in improving glycaemic control with the various basal insulin analogues. Studies comparing insulin glargine U100 with detemir U100, glargine U300 and degludec U100 found no notable differences in mean daily glucose levels and rates of hypoglycaemia during the hospital stay[60,63,64].

Non-insulin therapy in non-ICU settings. Few randomized controlled trials have reported the efficacy and safety of non-insulin

glucose-lowering agents in hospitalized patients in non-ICU settings. Despite the widespread use of these agents outside the hospital setting, there are limitations and necessary precautions on their use in hospital settings, especially given the limited number of published reports. Oral anti-diabetes medications, including metformin, sulfonylureas, SGLT2i, DPP4 inhibitors, glucagon-like peptide 1 (GLP1) receptor agonists (GLP1RAs) and thiazolidinediones have been, and continue to be, used in various countries and regions worldwide[65–67]. A study on diabetic drug utilization patterns in hospitalized patients with T2DM in New Delhi, India, revealed the everyday use of metformin, sulfonylureas, thiazolidinediones, insulin and α-glucosidase inhibitors[68]. However, a multicentre review of 11 UK trusts found a higher frequency of hypoglycaemia in sulfonylurea-treated inpatients when compared with insulin-treated individuals[65]. Sulfonylureas increase the risk of hypoglycaemia in patients with poor appetite or prescribed dietary restrictions, and can lead to prolonged hypoglycaemia in patients with impaired kidney function (Table 2). Similarly, metformin should be avoided in patients with acute congestive heart failure, severe renal or liver dysfunction, hypoperfusion or chronic pulmonary disease[69]. The use of thiazolidinediones should be restricted, as they have a slow onset of action and might precipitate or worsen congestive heart failure and peripheral oedema owing to fluid retention.

Increasing evidence from randomized controlled trials indicates that treatment with DPP4 inhibitors, either alone or in combination with basal insulin, is safe and effective in general medicine and surgery patients with mild to moderate hyperglycaemia[33,48]. The Sita-Hospital trial, a multicentre study in five hospitals in the USA in patients with T2DM in general medicine or surgery previously treated with oral anti-diabetes agents or low-dose insulin (<0.6 units/kg/day), found that a combination of the DPP4 inhibitor sitagliptin plus basal insulin resulted in similar glycaemic control, hypoglycaemia rates, hospital length-of-stay and hospital complications to the more labour-intensive basal–bolus insulin regimen[48]. A pooled analysis from three prospective studies of DPP4 inhibitors in patients with T2DM in general medicine or surgery showed no differences in mean hospital daily blood levels of glucose, percentage of glucose readings within the target range of 3.9–10 mmol/l (70–180 mg/dl) and length of stay following treatment with DPP4 inhibitors alone, DPP4 inhibitors in combination with basal insulin, or a basal–bolus regimen; however, there were fewer cases of hypoglycaemia following treatment with DPP4 inhibitors alone compared with their use with basal insulin or in a basal–bolus insulin regimen[70].

Randomized controlled studies have indicated that the use of SGLT2i in the hospital environment is a safe approach, provided that there is adequate monitoring[71,72]. In two large studies in patients admitted to hospital with COVID-19, treatment with empagliflozin and dapagliflozin, aimed at reducing organ failure in these patients, was well tolerated; however, these agents did not result in a notable reduction in the risk of organ dysfunction or mortality compared with placebo[71,73]. The most substantial evidence supporting the use of SGLT2i comes from its use in patients admitted to hospital with heart failure. The ADA recommends the initiation or continuation of these agents in hospitalized patients with heart failure after resolution of their critical illness if not contraindicated[3]. The EMPULSE (empagliflozin in patients hospitalized with acute heart failure who have been stabilized) study randomized 530 patients hospitalized with either acute or chronic heart failure within 3 days of hospitalization to empagliflozin or placebo and followed them for up to 90 days[74]. A statistically significant improvement in a composite score, including death from any cause and the number of heart failure events, was found in response to empagliflozin compared with placebo. Of the study participants, 46.8% had diabetes mellitus. The clinical benefit of empagliflozin in terms of all-cause death and heart failure events, as well as an improvement in quality of life, was similar in individuals with and without diabetes mellitus (weighted ratio 1.47 versus 1.3). However, real-world data on the use of these agents in the hospital are still needed, considering the small number of participants involved in these studies[75]. In addition, the glycaemic effects of SGLT2i in trials in inpatients have not been extensively reported. A systematic review and meta-analysis of randomized placebo-controlled trials showed no increased risk of hypoglycaemia with SGLT2i use compared with placebo[76], whereas a 20% reduction in the daily dose of insulin was found in a trial of SGLT2i therapy in patients hospitalized for heart failure[77]. Finally, it is important to note that the use of SGLT2i should be closely monitored in hospital settings in individuals who are nil-by-mouth or have very low carbohydrate intake, owing to the increased risk of diabetic ketoacidosis[78]. A decision to start SGLT2i in the hospital setting for heart failure should prompt mitigation strategies, such as monitoring for acidosis and ketones and screening for urinary tract infections in high-risk patients.

The use of GLP1RAs, alone or in combination with basal insulin, can improve glycaemic control compared with the basal–bolus insulin regimen, although the data are limited[51,74]. A multicentre, open-label, randomized trial studied the safety and efficacy of the GLP1RA exenatide alone or in combination with basal insulin compared with basal–bolus insulin therapy in hospitalized patients. Exenatide plus basal insulin resulted in a lower mean daily blood concentration of glucose than basal insulin or exenatide alone ($P = 0.02$)[51]. The American Society of Anaesthesiologists task force on preoperative fasting has recommended withholding therapy either the day before or on the day of the procedure in question in patients receiving short-acting GLP1RAs and for 1 week in patients on weekly dosing GLP1RAs before surgery and any procedure that involves deep sedation[79]. This recommendation was supported mainly by case reports and retrospective studies that showed an increased risk of retained gastric contents, regurgitation and pulmonary aspiration following treatment with GLP1RAs. However, large observational studies found no differences

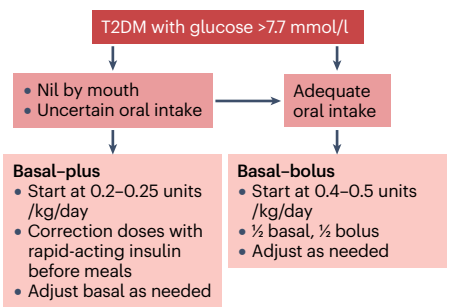
T2DM with glucose >7.7 mmol/l
• Nil by mouth
• Uncertain oral intake
Adequate oral intake
Basal–plus
• Start at 0.2–0.25 units /kg/day
• Correction doses with rapid-acting insulin before meals
• Adjust basal as needed
Basal–bolus
• Start at 0.4–0.5 units /kg/day
• ½ basal, ½ bolus
• Adjust as needed

Fig. 2 | Basal-plus and basal–bolus insulin regimens for the management of general medicine and surgery patients with type 2 diabetes mellitus. Individuals with reduced calorie intake can be treated with a basal insulin analogue (such as glargine, detemir or degludec) once daily or with neutral protamine Hagedorn (NPH) twice daily at a starting dose of 0.2–0.25 units/kg plus insulin correction (basal-plus). Those patients on a regular diet or not controlled with basal treatment alone can be treated with a basal–bolus regimen, starting at 0.4–0.5 units/kg/day, given 50% as basal and 50% as insulin before meals (bolus). T2DM, type 2 diabetes mellitus. Adapted from ref. 41, Springer Nature Limited.

in pulmonary aspiration or complications with the preoperative use of these agents[80]. In addition, the Society for Perioperative Assessment and Quality Improvement Expert Consensus Statement indicated that the perioperative use of GLP1RAs should depend on the specific agent, dosing schedule, fasting time, gastrointestinal symptoms and type of surgery[81]. It is our opinion that interrupting GLP1RA therapy might not confer much benefit in terms of decreasing the risk of aspiration pneumonia because of the long washout time needed to resolve the effects on gastric emptying, and could lead to the loss of glycaemic-lowering effects peri-surgery and increase the risk of cardiovascular events that is often seen in patients with T2DM whose medication is interrupted. GLP1RAs should be stopped in patients who have not been using them chronically or who are in dose-escalation phases and have notable symptoms of fullness, nausea and vomiting. In any case, the first and most crucial intervention is to change the duration of fasting for solids and possibly also for liquids before surgery. Data from the real world and gastric emptying studies support the implementation of a clear liquid diet for 24 h before anaesthesia. For symptomatic patients with gastrointestinal symptoms or those who have not been on clear liquids for 24 h, gastric ultrasonography might help to guide decisions. Collaboration with the prescribing clinicians is essential when making decisions.

Nutritional support

Hyperglycaemia is a frequent complication of nutritional support (enteral and parenteral feeding) in hospitalized patients with and without diabetes mellitus and has been associated with an increased risk of infectious complications[82]. No specific guidelines recommend glycaemic targets and effective strategies for managing hyperglycaemia during periods of specialized nutritional support. Managing hyperglycaemia in hospitalized patients with diabetes mellitus receiving specialized nutritional support should include optimizing carbohydrate content as well as intravenous or subcutaneous insulin therapy if appropriate.

Nutritional support regimens can take several different forms, including a cyclical method, where feeding is provided at a specific time or during a certain period of each day (for example, overnight); continuously; or combined with other forms of feeding. In patients receiving nutritional support, it is important to synchronize the delivery of nutrition with subcutaneous or intravenous insulin treatment to match the physiological action of insulin.

Enteral feeding

The administration of subcutaneous long-acting basal insulin with scheduled or corrective doses of short-acting insulin is superior to the sliding scale insulin strategy in patients receiving enteral feedings. Basal insulin can be provided subcutaneously as intermediate-acting insulin (NPH insulin given twice daily) or long-acting insulin (glargine or detemir given once daily). Prandial and correction insulin can be given as regular or rapid-acting insulin every 4–6 h[83].

Parenteral feeding

Many patients with or without diabetes mellitus admitted to ICU and non-ICU settings are unable to receive oral or enteric nutrition and instead require parenteral nutritional support (intravenous feeding). Hyperglycaemia is frequently observed during parenteral nutrition and is associated with a higher risk of in-hospital complications compared with patients who have levels of glucose in the blood of <6.7 mmol/dl (120 mg/dl)[84]. In critically ill patients, administering intravenous insulin provides the safest option for controlling blood levels of glucose and avoiding hypoglycaemia[85]. For patients receiving continuous or cyclical parenteral feeding in a general ward, regular insulin can be added to the solution, starting at the standard dose of 1 unit per 10 g of dextrose content. If hyperglycaemia persists, correctional rapid-acting or regular insulin should be administered subcutaneously. Adding a small dose of long-acting insulin might also offer benefits, particularly in patients who are receiving cyclical parenteral nutritional, while monitoring for hypoglycaemia[27,86,87].

Patients on glucocorticoids

Glucocorticoids can be associated with severe hyperglycaemia in the hospital setting, and severe hyperglycaemia has been reported in 56–86% of patients with and without a diagnosis of diabetes mellitus receiving glucocorticoid treatment[88]. Despite the common use of glucocorticoids in hospitals, data from well-designed clinical trials are lacking, making it challenging to determine the optimal insulin regimen in patients receiving this type of medication[4,89]. Glucocorticoids increase insulin resistance and stimulate gluconeogenesis, resulting in an increase in glucose levels postprandially[90]. A standard treatment approach in patients with glucocorticoid-induced hyperglycaemia on once-daily or twice-daily glucocorticoid treatment could include pairing the administration of NPH insulin with the hyperglycaemic response to prednisone or prednisolone, based on the known induction of a peak in the plasma levels of glucose 4–6 h after the administration of these glucocorticoids[91]. The use of a basal–bolus insulin regimen or basal plus correction doses before meals or every 6 h in the nil-by-mouth state has also been effective in managing hyperglycaemia in patients receiving high-dose steroids[92]. In a retrospective study of data from 18,599 patient-days from electronic health records in an academic centre, increasing the insulin to steroid ratios was found to be positively associated with glycaemic control and hypoglycaemia[88]. The study suggested that an insulin to steroid ratio of approximately 0.3 units/kg per 10 mg prednisone equivalent dose is optimal for low-dose and medium-dose steroids, and 0.1 units/kg per 10 mg prednisone equivalent dose for high-dose steroids to reach optimal glucose control while minimizing hypoglycaemia[88].

Technology for glucose monitoring and management

Advances in technology over past decades have revolutionized patient care and the management of diabetes mellitus in the hospital setting. The use of continuous glucose monitoring (CGM), continuous subcutaneous insulin infusion (insulin pump therapy) and automated insulin delivery (AID) systems is growing in the ambulatory and inpatient settings. Experts and medical societies agree that CGM offers benefits over intermittent capillary blood glucose testing by preventing severe hyperglycaemia and hypoglycaemia by identifying glucose trends and allowing for more accurate insulin adjustments[93–95]. Several clinical guidelines on diabetes mellitus support the continued use of outpatient continuous subcutaneous insulin infusion in individuals who can physically manage their insulin pumps during hospitalization. However, randomized controlled trials are needed to determine whether CGM and continuous subcutaneous insulin infusion approaches in the hospital setting can improve clinical outcomes compared with traditional methods such as finger-stick (capillary point-of-care) glucose monitoring and insulin injections[28].

Continuous glucose monitoring in the hospital setting

Capillary point-of-care glucose testing is the standard for glucose monitoring in hospitalized patients with diabetes mellitus and is typically

performed three to four times daily. However, point-of-care testing poses limitations owing to its intermittent nature, resulting in periods when the blood glucose level is not known (especially overnight), as well as the associated time burden on both the patient and hospital staff. CGM technology, which provides estimated glucose values every 1–5 min and tracks glucose trends, offers a comprehensive assessment of glycaemic control. Additionally, CGM is more reliable and accurate in the inpatient setting compared with point-of-care testing and laboratory values[96,97]. A study using intermittently scanned CGM found a mean absolute relative difference (MARD) of 14.8% and an error grid analysis of 98.8% of glucose pairs within zones A and B in patients with T2DM admitted to general medicine and surgery[97]. A different analysis of data from three inpatient studies (n = 4,067 matched glucose pairs) found a similar MARD of 12.8% and error grid analysis of 98.7% of all values in zones A and B using real-time CGM[96]. The accuracy of CGM in ICU settings was assessed in a scoping review involving 96 studies. The authors of the review concluded that the MARD of the newer factory-calibrated subcutaneous CGM devices varied from 9.7% to 20%; the MARD of intravenous CGM devices was 5–14.2%[98].

The close monitoring of glucose levels offered by CGM can decrease the incidence of hypoglycaemia in hospital settings. A statistically significant reduction in hypoglycaemia was observed with real-time CGM compared with point-of-care testing in patients admitted to the ICU requiring mechanical ventilation[99]. Several other studies in the ICU setting have found that, compared with intermittent capillary blood glucose monitoring, CGM can offer benefits in terms of identifying and preventing severe hyperglycaemia and hypoglycaemia by enabling insulin infusions to be adjusted more rapidly and more accurately[100,101]. On the other hand, another study found no notable differences in glycaemic control between CGM combined with an enhanced model predictive control insulin titration algorithm and standard point-of-care glucose testing in patients admitted to ICU following cardiac surgery[102,103].

In non-critically ill hospitalized patients, two studies showed no difference in improving glycaemic control between CGM and capillary point-of-care testing[103,104]. However, other studies showed that CGM is more effective at detecting hypoglycaemia, including asymptomatic and nocturnal hypoglycaemia, than capillary glucose testing[97,105,106]. CGM was found to detect more hypoglycaemic events than did point-of-care testing in non-critically ill patients with T2DM on basal–bolus insulin regimens[105], and the feasibility of transmitting CGM data to nursing personnel in a telemetry-type method to successfully prevent potential hypoglycaemic episodes was also reported[106] (Fig. 3a).

The ADA and Endocrine Society guidelines have suggested that, in patients with diabetes mellitus who use a personal CGM device, the device should continue to be used during hospitalization if clinically appropriate, with confirmatory measurements for insulin dosing and hypoglycaemia assessment[27,28]. However, despite increasing evidence from observational and randomized controlled studies indicating the safety and efficacy of real-time CGM in the hospital setting[107], the initiation of inpatient CGM devices during hospitalization has not been approved by the FDA.

Despite the advantages of CGM, several potential contraindications and limitations exist regarding the use of CGM devices. These shortcomings include patient-related factors (for example, hypovolaemia or a reduced level of consciousness) and device-related factors (for example, using the device in an MRI scanner or in situations where the individual's positioning could compress the device or make access difficult). Surgery-related issues involve using diathermy for procedures,

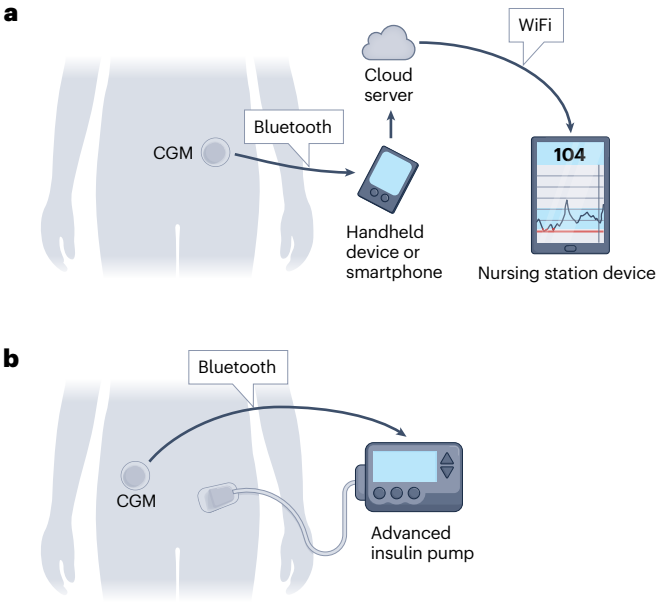

Fig. 3 | The use of advanced technology for managing diabetes mellitus in the hospital setting. a, Real-time glucose monitoring in the hospital. A continuous glucose monitoring (CGM) device is attached to the patient and blood glucose values are transmitted every 1–5 min using Bluetooth technology to a hand-held device or a smart phone; these CGM data can also be stored in the cloud. A separate device placed at the nursing station shows glucose values directly from the CGM cloud. **b**, The automated insulin delivery system consists of a real-time CGM device that is connected to an advanced insulin pump that has the ability to adjust insulin administration according to the blood glucose values recorded by the monitoring device.

or surgical teams who are unfamiliar with the technology[108]. Other hospital-related factors also exist: for example, there are currently insufficient endocrinologists or trained professionals to understand CGM systems, interpret CGM traces, and adjust diabetes mellitus management in the hospital setting. A basic CGM curriculum could be added to formal education in nursing schools as well as to formal medicine residencies. Other limitations include educating staff on the difference between CGM and point-of-care testing, device and connectivity troubleshooting and CGM applications. These obstacles and others were addressed in a 2024 consensus statement for the use of CGM systems in hospital settings[109].

Closed loops and AIDs in the hospital setting

The integration of CGMs and insulin delivery devices in outpatient settings has seen considerable growth over the past 10 years. However, using these closed-loop systems for safe, efficient and effective inpatient care is a relatively new concept[110] (Fig. 3b). Pilot studies have shown that these devices can improve glycaemic outcomes, resulting in a greater time in range and fewer hypoglycaemic episodes than conventional subcutaneous insulin therapy[110,111]. These benefits extend to patients receiving nutritional support, despite the complexities of the management of inpatient diabetes mellitus, such as rapid changes in clinical status, variable food intake, and the use of medications such as glucocorticoids that interfere with carbohydrate metabolism, leading to high variability in daily insulin requirements[112].

A feasibility study explored the use of AID systems with remote glucose monitoring in a hospital setting. This single-arm multicentre pilot trial evaluated the technology in participants with insulin-requiring diabetes mellitus on non-ICU medical–surgical units. The participants were satisfied with the use of the AID system and there were no incidences of diabetic ketoacidosis or severe hypoglycaemia; the 16 participants achieved an overall time-in-range of 68 ± 16%, with 0.17 ± 0.3% of the time with blood glucose levels of <70 mg/dl and 0.06 ± 0.2% of the time with levels of <54 mg/dl[113].

Conclusions

There have been notable advances in managing inpatient hyperglycaemia and diabetes mellitus over the past 20 years. The management approach has evolved from a reactive method, characterized by waiting for hyperglycaemia to be noted and using sliding scale insulin alone, to a more proactive strategy involving increased screening and more physiological treatments with intravenous and basal–bolus insulin therapy. Early guidelines did not recommend the use of oral anti-diabetes agents in the inpatient setting owing to a lack of safety and efficacy studies. However, increasing evidence indicates that treatment with oral agents, such as DPP4 inhibitors, whether alone or combined with basal insulin, is safe and effective for general medicine and surgery patients with mild-to-moderate hyperglycaemia. The past 10 years have seen a shift towards incorporating advanced technology into the management of diabetes mellitus. As we progress into a new technological era, future studies are needed to validate the benefits of CGM and AID systems in the hospital setting.

Published online: 04 August 2025

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Acknowledgements
G.E.U. acknowledges the support of research grants from the US National Institutes of Health (NATS UL 3UL1TR002378-05S2), from the Clinical and Translational Science Award Program and the NIH and National Center for Research Resources (NIH/National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) 2P30DK111024-06).

Author contributions
T.I., I.C.-R., K.K.D. and G.E.U. researched data for the article, contributed substantially to discussion of the content and wrote the article. T.I., K.K.D., L.H. and G.E.U. reviewed and/or edited the manuscript before submission.

Competing interests
T.I. has received research support (paid to Emory University) from AbbVie. G.E.U. has received research support (paid to Emory University) from Bayer, Abbott, Dexcom and Corcept, and has served as a member of advisory boards for Dexcom, Mankind, Glucotrack, Corcept and GlyCare. K.K.D. has received honoraria for travel, advisory boards and speaker fees from Abbott Diabetes, AstraZeneca, Boehringer Ingelheim, Novo Nordisk, Eli Lilly, Menarini and Sanofi Diabetes. I.C.-R. and L.H. declare no competing interests.

Additional information

Peer review information *Nature Reviews Endocrinology* thanks Mikkel B. Christensen, who co-reviewed with Iben Rix; Peter Lommer Kristensen; and Mervyn Kyi for their contribution to the peer review of this work.

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